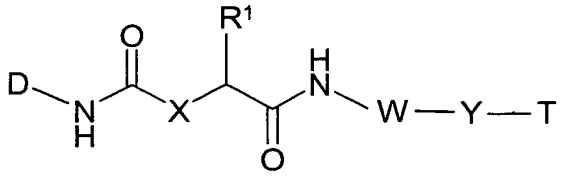
Patent Claims

1. Compounds of the formula I



I

in which

D denotes an aromatic five-membered heterocyclic ring having 1 to 4 N, O and/or S atoms which is unsubstituted or mono- or polysubstituted by Hal, A, OR^2, $N(R^2)_2$, NO_2, CN, $COOR^2$ or $CON(R^2)_2$,

X denotes NR^3 or O,

R^1 denotes H, Ar, Het, cycloalkyl or A, which may be substituted by OR^2, SR^2, $N(R^2)_2$, Ar, Het, cycloalkyl, CN, $COOR^2$ or $CON(R^2)_2$,

R^2 denotes H, A, $-[C(R^3)_2]_n$-Ar, $-[C(R^3)_2]_n$-Het, $-[C(R^3)_2]_n$-cycloalkyl, $-[C(R^3)_2]_n-N(R^3)_2$ or $-[C(R^3)_2]_n-OR^3$,

R^3 denotes H or A,

W denotes $-[C(R^3)_2]_n-$,

Y denotes alkylene, cycloalkylene, Het-diyl or Ar-diyl,

T denotes a mono- or bicyclic saturated, unsaturated or aromatic carbo- or heterocyclic ring having 0 to 4 N, O and/or S atoms, which may be unsubstituted or mono-, di- or trisubstituted by Hal, A, $-[C(R^3)_2]_n$-Ar, $-[C(R^3)_2]_n$-Het, $-[C(R^3)_2]_n$-cycloalkyl, OR^3, $N(R^3)_2$, NO_2, CN, $COOR^2$, $CON(R^2)_2$, NR^2COA, $NR^2CON(R^2)_2$, NR^2SO_2A, COR^2, SO_2NR^2 and/or $S(O)_mA$ and/or carbonyl oxygen, or $N(R^2)_2$

and, if Y = piperidine-1,4-diyl, also R^2 or cycloalkyl,

A denotes unbranched or branched alkyl having 1-10 C atoms, in which one or two CH_2 groups may be replaced by O or S atoms and/or by -CH=CH- groups and/or also 1-7 H atoms may be replaced by F,

Ar denotes phenyl, naphthyl or biphenyl, each of which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OR^3, $N(R^3)_2$, NO_2, CN, $COOR^3$, $CON(R^3)_2$, NR^3COA, $NR^3CON(R^3)_2$, NR^3SO_2A, COR^3, $SO_2N(R^3)_2$, $S(O)_mA$, $-[C(R^3)_2]_n-COOR^{2'}$ or $-O-[C(R^3)_2]_o-COOR^{2'}$,

$R^{2'}$ denotes H, A, $-[C(R^3)_2]_n-Ar'$, $-[C(R^3)_2]_n-Het'$, $-[C(R^3)_2]_n-$cycloalkyl, $-[C(R^3)_2]_n-N(R^3)_2$ or $-[C(R^3)_2]_n-OR^3$,

$R^{2''}$ denotes H, A, $-[C(R^3)_2]_n-Ar'$ or $-[C(R^3)_2]_n-$cycloalkyl, $-[C(R^3)_2]_n-N(R^3)_2$ or $-[C(R^3)_2]_n-OR^3$,

Ar' denotes phenyl or benzyl, each of which is unsubstituted or mono- or disubstituted by Hal or A,

Het denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocyclic ring having 1 to 4 N, O and/or S atoms, which may be unsubstituted or mono-, di- or trisubstituted by carbonyl oxygen, =S, $=N(R^3)_2$, Hal, A, $-[C(R^3)_2]_n-Ar$, $-[C(R^3)_2]_n-Het^1$, $-[C(R^3)_2]_n-$cycloalkyl, $-[C(R^3)_2]_n-OR^{2'}$, $-[C(R^3)_2]_n-N(R^{2'})_2$, NO_2, CN, $-[C(R^3)_2]_n-COOR^{2'}$, $-[C(R^3)_2]_n-CON(R^{2'})_2$, $-[C(R^3)_2]_n-NR^{2'}COA$, $NR^{2'}CON(R^{2'})_2$, $-[C(R^3)_2]_n-NR^{2'}SO_2A$, $COR^{2'}$, $SO_2NR^{2'}$ and/or $S(O)_mA$,

Het^1 denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocyclic ring having 1 to 2 N, O and/or S atoms, which may be unsubstituted or mono- or disubstituted by carbonyl oxygen, =S, $=N(R^3)_2$, Hal, A, $OR^{2''}$, $N(R^{2''})_2$, NO_2, CN, $COOR^{2''}$, $CON(R^{2''})_2$, $NR^{2''}COA$, $NR^{2''}CON(R^{2''})_2$, $NR^{2''}SO_2A$, $COR^{2''}$, $SO_2NR^{2''}$ and/or $S(O)_mA$,

Hal denotes F, Cl, Br or I,

n denotes 0, 1 or 2,

m denotes 0, 1 or 2,

o denotes 1, 2 or 3,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1,
in which

D denotes an aromatic five-membered heterocyclic ring having 1 to 2 N, O and/or S atoms which is unsubstituted or mono- or disubstituted by Hal,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2,
in which

D denotes a thienyl ring which is mono- or disubstituted by Hal,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3 ,
in which

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4,
in which

R^1 denotes H or unsubstituted phenyl, thienyl or alkyl having 1-6 C atoms,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5,

in which

X denotes NH or O,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1-6, in which

W denotes $(CH_2)_n$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1-7, in which

Y denotes Ar-diyl or Het-diyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8, in which

T denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocyclic ring having 1 to 2 N and/or O atoms, which may be unsubstituted or mono- or disubstituted by carbonyl oxygen,

or $N(R^2)_2$

and, if Y = piperidine-1,4-diyl, also R^2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to one or more of Claims 1-9, in which

T denotes a mono- or bicyclic saturated or unsaturated heterocyclic ring having 1 to 2 N and/or O atoms which is mono- or disubstituted by carbonyl oxygen (=O),
or $N(R^2)_2$
and, if Y = piperidine-1,4-diyl, also R^2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

11. Compounds according to one or more of Claims 1-10, in which

T denotes piperidin-1-yl, pyrrolidin-1-yl, 1*H*-pyridin-1-yl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, 2*H*-pyridazin-2-yl, pyrazin-1-yl, azepan-1-yl, 2-azabicyclo[2.2.2]octan-2-yl, each of which is mono- or disubstituted by carbonyl oxygen, or $N(R^2)_2$
and, if Y = piperidine-1,4-diyl, also R^2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

12. Compounds according to one or more of Claims 1-11, in which

Ar denotes phenyl which is unsubstituted or mono- or disubstituted by Hal, A, OA, SO_2A, $COOR^2$, SO_2NH_2 or CN,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

13. Compounds according to one or more of Claims 1-12, in which

D denotes an aromatic five-membered heterocyclic ring having 1 to 2 N, O and/or S atoms which is unsubstituted or mono- or disubstituted by Hal,

R^1 denotes H or unsubstituted phenyl, thienyl or alkyl having 1-6 C atoms,

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

X denotes NH or O,

W denotes W $(CH_2)_n$,

Y denotes Ar-diyl, pyridinediyl or piperidinediyl,

Ar denotes phenyl which is unsubstituted or mono- or disubstituted by Hal, A, OA, SO_2A, $COOR^2$, SO_2NH_2 or CN,

T denotes piperidin-1-yl, pyrrolidin-1-yl, 1*H*-pyridin-1-yl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, 2*H*-pyridazin-2-yl, pyrazin-1-yl, azepan-1-yl, 2-azabicyclo[2.2.2]octan-2-yl, each of which is mono- or disubstituted by carbonyl oxygen, or $N(R^2)_2$

and, if Y = piperidine-1,4-diyl, also R^2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

14. Compounds according to one or more of Claims 1-13, in which

D denotes thienyl, thiazolyl or furyl, each of which is mono- or disubstituted by Hal,

R^1 denotes H or unsubstituted phenyl, thienyl or alkyl having 1-6 C atoms,

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

X denotes NH or O,

W denotes W $(CH_2)_n$,

Y denotes Ar-diyl, pyridinediyl or piperidinediyl,

Ar denotes phenyl which is unsubstituted or mono- or disubstituted by Hal, A, OA, SO_2A, $COOR^2$, SO_2NH_2 or CN,

T denotes piperidin-1-yl, pyrrolidin-1-yl, pyridinyl, morpholin-4-yl, piperazin-1-yl, 1,3-oxazolidin-3-yl, pyridazin-2-yl, pyrazinyl,

azepan-1-yl, 2-azabicyclo[2.2.2]octan-2-yl, each of which is unsubstituted or mono- or disubstituted by carbonyl oxygen, or $N(R^2)_2$

and, if Y = piperidine-1,4-diyl, also R^2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

15. Compounds according to Claim 1 selected from the group

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]valeramide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)-3-methylphenyl]valeramide,

2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]acetamide,

(R)-2-[3-(5-bromothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]valeramide,

(R)-2-[3-(5-bromofuran-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]valeramide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-2-phenylacetamide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-2-(thiophen-2-yl)acetamide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(2-oxopiperidin-1-yl)phenyl]valeramide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(2-oxo-1*H*-pyrazin-1-yl)phenyl]valeramide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[2-oxo-3,4,5,6-tetrahydro-[1,2']bipyridinyl-5'-yl]valeramide,

(S)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-2-phenylacetamide,

(R)-2-[3-(5-chlorothiophen-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenylmethyl]valeramide,

(R)-2-[3-(5-chlorothiazol-2-yl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]valeramide,

(R)-2-[N-(5-chlorothiophen-2-yl)carbamoyloxy]-N-[[4-(3-oxo-morpholin-4-yl)phenyl]valeramide,

(R)-2-[*N*-(5-chlorothiophen-2-yl)carbamoyloxy]-*N*-[*C*-(3,4,5,6-tetrahydro-2*H*-[1,4']bipyridinyl-4-yl)methyl]valeramide,

(R)-2-[N-(5-chlorothiophen-2-yl)carbamoyloxy]-N-[1-isopropyl-piperidin-4-ylmethyl]-2-phenylacetamide,

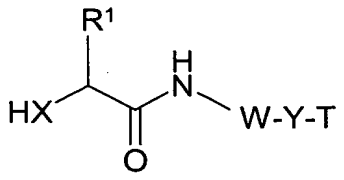
(R)-2-[N-(5-chlorothiophen-2-yl)carbamoyloxy]-N-[[4-(morpholin-4-yl)phenyl]valeramide

(R)-2-[N-(5-chlorothiophen-2-yl)carbamoyloxy]-N-(4-dimethyl-aminophenyl)-2-phenylacetamide

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

16. Process for the preparation of compounds of the formula I according to Claims 1-15 and pharmaceutically usable derivatives, solvates and stereoisomers thereof, characterised in that

a) a compound of the formula II



II

in which

R^1, W, X, Y and T have the meaning indicated in Claim 1,

is reacted with a compound of the formula III

D-N=C=O III

in which

D has the meaning indicated in Claim 1,

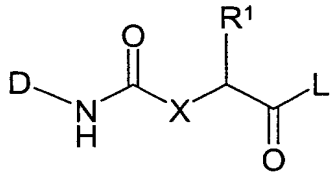
or

b) a compound of the formula IV

H_2N-W-Y-T IV

in which W, Y and T have the meaning indicated in Claim 1,

is reacted with a compound of the formula V



V

in which

L denotes Cl, Br, I or a free or reactively functionally modified OH group, and

R^1, X and D have the meanings indicated in Claim 1,

and/or

a base or acid of the formula I is converted into one of its salts.

17. Compounds of the formula I according to one or more of Claims 1 to 15 as inhibitors of coagulation factor Xa.

18. Compounds of the formula I according to one or more of Claims 1 to 15 as inhibitors of coagulation factor VIIa.

19. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 15 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

20. Medicamens comprising at least one compound of the formula I according to one or more of Claims 1 to 15 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

21. Use of compounds according to one or more of Claims 1 to 15 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases.

22. Set (kit) consisting of separate packs of
(a) an effective amount of a compound of the formula I according to one or more of Claims 1 to 15 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios,
and
(b) an effective amount of a further medicament active ingredient.

23. Use of compounds of the formula I according to one or more of Claims 1 to 15 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios,

for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases, in combination with at least one further medicament active ingredient.